Deep learning for medical imaging school 2021



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Weakly Supervised CNN Segmentation: Models and Optimization

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Why weak supervision is interesting?

Deep CNNs are dominating computer vision e.g., semantic segmentation



Cordts et al., "The Cityscapes Dataset for Semantic Urban Scene Understanding," CVPR 2016

... and medical image analysis



But, massive and dense annotations are not always available

Full supervision

 more than 1h per image (even several hours for a medical image)



 Bottleneck for learning at large scale



Weak supervision (e.g., image-level tags)



 Scalable for large numbers of labels

• 1s per label per

image

person horse background

Semi-supervision with a lot of **non-annotated** data, and a **fraction** of points annotated



Full annotations

Semi-supervised

Figures from Lin et al. Scribblesup: Scribble-supervised convolutional networks for semantic segmentation, CVPR 2016 6

Forms of semi/weak supervision: Examples in segmentation



Forms of semi/weak supervision: Examples in segmentation



[Marin et al., CVPR 2019], [Tang et al., ECCV 2018], [Lin et al., CVPR 2016], [Khoreva et al. CVPR 2017], [Vernaza et al., CVPR 2017], [Kolesnikov and Lampert, ECCV 2016] [Dai et al., CVPR 2015], [Bearman et al., ECCV 2016] [Pathak et al., ICCV 2015], [Papandreou et al., ICCV 2015]

[Rajchl et al., TMI 2017] [Bai et al., MICCAI 2017] [Kervadec et al., MedIA]

Full annotations are much more problematic in medical imaging

Not anywhere close to the 10k images of Pascal VOC and the 5k of Cityscapes

Crowdsourcing?

Select all images with esophagus Click verify once there are none left.



C 🗋 🛈



Full annotations are much more problematic in medical imaging

Not anywhere close to the 10k images of Pascal VOC and the 5k of Cityskapes

Crowdsourcing?

Select all images with esophagus Click verify once there are none left.



Dense 3D annotations: several hours (of radiologist time)



C 🗋 🛈



Domain shifts make things worse (even with full annotations in one domain)



[MRI Prostate segmentation: Figure from Zhu et al., Boundary-weighted Domain Adaptive Neural Network for Prostate MR Image Segmentation ArXiv 2019]

Domain shifts: within and across modalities



[Images from Dou et al., PnP-AdaNet: Plug-and-play adversarial domain adaptation network with a benchmark at cross-modality cardiac segmentation ArXiv 2018]

Unsupervised domain adaptation



Bad generalization to the target



[Images from Dou et al., PnP-AdaNet: Plug-and-play adversarial domain adaptation network with a benchmark at cross-modality cardiac segmentation ArXiv 2018]

A lot of interest in vision as well: Domain shifts are *everywhere* **BUT** we cannot label *everywhere*



Figures from [Zhang et al., A Curriculum Domain Adaptation Approach to the Semantic Segmentation of Urban Scenes TPAMI 2019]

A lot of interest in vision as well: Domain shifts are *everywhere* **BUT** we cannot label *everywhere*



Cityscapes (5000 images): labeling of 1 image takes 90 min at average [Cordt et al., CVPR 2016] 16

UDA = SSL + domain shift



Surprisingly in medical image analysis, we are behind



Semi/weak supervision in a nutshell: We are leveraging **unlabelled** data with **priors**

• Structure-driven priors: *Regularization (Part 1)*

• Knowledge- and data-driven priors (Part 2)

Part 1

Regularization

Laplacian (and CRFs)

Semi-supervised learning (general form)



Semi-supervised learning (general form)



Semi-supervised learning (general form)







(softmax outputs of the network)



e.g.: simplex probability vectors (*softmax outputs of the network*)

- [weston et al., Deep Learning via semi-supervised embedding, ICML 2008]
- [Belkin et al., Manifold regularization: a geometric framework for learning from Labeled and Unlabeled Examples, JMLR 2006]
- [Zhu et al., Semi-Supervised Learning Using Gaussian Fields and Harmonic Functions, ICML 2003]

$$\min_{\theta} \sum_{p \in \mathcal{L}} l(\mathbf{y}^p, \mathbf{s}^p_{\theta}) + \sum_{p, q \in \mathcal{L} \cup \mathcal{U}} w_{p,q} \left\| \mathbf{s}^p_{\theta} - \mathbf{s}^q_{\theta} \right\|^2$$



[Tang et al., On regularized losses for weakly supervised segmentation, ECCV 2018]

$$\min_{\theta} \sum_{p \in \mathcal{L}} l(\mathbf{y}^p, \mathbf{s}^p_{\theta}) + \sum_{p, q \in \mathcal{L} \cup \mathcal{U}} w_{p, q} \|\mathbf{s}^p_{\theta} - \mathbf{s}^q_{\theta}\|^2$$



On the vertices of the simplex (binary variables), this is exactly the Potts model in Conditional Random Fields (e.g., Dense CRFs)!

[Tang et al., On regularized losses for weakly supervised segmentation, ECCV 2018]





[Tang et al., On regularized losses for weakly supervised segmentation, ECCV 2018] [Marin et al., Beyond gradient descent for regularized segmentation losses, CVPR 2019]

$$\min_{\theta} \sum_{p \in \mathcal{L}} l(\mathbf{y}^p, \mathbf{s}^p_{\theta}) + \sum_{p, q \in \mathcal{L} \cup \mathcal{U}} w_{p,q} \left\| \mathbf{s}^p_{\theta} - \mathbf{s}^q_{\theta} \right\|^2$$



The exciting part in this plot:

Dense CRF with SGD gets you 97.6% of full supervision performance with 3% of the labels!

[Tang et al., On regularized losses for weakly supervised segmentation, ECCV 2018] [Marin et al., Beyond gradient descent for regularized segmentation losses, CVPR 2019]

$$\min_{\theta} \sum_{p \in \mathcal{L}} l(\mathbf{y}^{p}, \mathbf{s}^{p}_{\theta}) + \sum_{p, q \in \mathcal{L} \cup \mathcal{U}} w_{p, q} \left\| \mathbf{s}^{p}_{\theta} - \mathbf{s}^{q}_{\theta} \right\|^{2}$$



The disturbing part (for those who know classical CRFs): Dense CRF is not supposed to be better than grid CRF

[Tang et al., On regularized losses for weakly supervised segmentation, ECCV 2018] [Marin et al., Beyond gradient descent for regularized segmentation losses, CVPR 2019]

Some applications of CRF loss in MICCAI

White (FN); Magenta (FP); Green (TP)



- Figures from Qu et al., Weakly Supervised Deep Nuclei Segmentation using Points Annotation in Histopathology Images, MIDL 2019 [Histology, point annotation]
- Ji et al., Scribble-Based Hierarchical Weakly Supervised Learning for Brain Tumor Segmentation, MICCAI 2019 [Brain tumor images, scribble annotations]

Regularization

entropy

Entropy minimization for SSL

 $\sum y^{p,c} \log s^{p,c}_{\theta}$ $\sum \sum s_{\theta}^{p,c}$ mi θ $p \in \mathcal{U} c = 1$ $p \in \mathcal{L} c = 1$

Shannon Entropies: "unsupervised cross-entropies (with unknown labels)"

- Grandvalet & Bengio, Semi-supervised learning by entropy minimization, NIPS 2005
- Gomes et al., Discriminative clustering by regularized information maximization, NIPS 2010

Effect of the entropy (why is it good for SSL?): It makes the predictions confident (like cross-entropy)


Entropy minimization for UDA



Images from Vu et al., ADVENT: Adversarial Entropy Minimization for Domain Adaptation in Semantic Segmentation, CVPR 2019

Entropy minimization for UDA



Entropy minimization for UDA



Images from Bateson et al., Source-relaxed domain adaptation for segmentation, MICCAI 2020

Why entropy minimization is good (It increases the margin between the classes)



High entropy (low confidence)



Low entropy (high confidence)

Effect of the entropy (why is it good for SSL?): It increases the margin between the classes



Image classification UDA on VisDA17 data set: Feature visualization for source model (left) and *min-entropy (lower bound on Shannon)* minimization (right) equivalent to self training (clarified in the next slide)

Figures from Zou et al., Confidence regularized self training, ICCV 2019

Difficulty of optimizing entropy



Difficulty of optimizing entropy



Difficulty of optimizing entropy

Typically we add other cues to facilitate optimization and avoid trivial solutions (more on this later)



$$Pr(c_2|d_p) = s^{p,2} = 1 - s^{p,1} = 1$$

$$Pr(c_1|d_p) = s^{p,1} = 1$$
Softmax output
Note: Ignoring the network parameters to simplify notation



Min entropy (max confidence)



This bad solution also has a minimum entropy!!!

Marginal probabilities of the labels -- Class proportion -- Region size (normalized) in segmentation

$$\Pr(c_1) \propto \sum s^{p,1}$$



I(X,Y) = H(Y) - H(Y/X)

MI = Entropy (label marginal) – Entropy (posterior)

Standard and old in clustering, e.g.,:

Gomes et al., Discriminative clustering by regularized information maximization, NIPS 2010



Standard and old in clustering: Gomes et al., Discriminative clustering by regularized information maximization, NIPS 2010



Other priors (learned, known)

Standard and old in clustering:

Gomes et al., Discriminative clustering by regularized information maximization, NIPS 2010



Other distances, relaxation of equality constraints

Standard and old in clustering:

Gomes et al., Discriminative clustering by regularized information maximization, NIPS 2010



Constrained CNNs

Knowledge vs data driven priors



Knowledge vs data driven priors













- Pathak et al., Constrained convolutional neural networks for weakly supervised segmentation, ICCV 2015
- Kervadec et al., Constrained-CNN losses for weakly supervised segmentation, MedIA 2019.

Image tags

Bounding boxes



Person Bike





Tumor



Original Image tags Bounding boxes

- Pathak et al., Constrained convolutional neural networks for weakly supervised segmentation, ICCV 2015
- Kervadec et al., Constrained-CNN losses for weakly supervised segmentation, MedIA 2019.



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- Pathak et al., Constrained convolutional neural networks for weakly supervised segmentation, ICCV 2015
- Kervadec et al., Constrained-CNN losses for weakly supervised segmentation, MedIA 2019.

Another data-driven priors

Image captions



A boy jumping on a skateboard

Extreme points



Image from Maninis et al, CVPR'18

• Maninis et al. Deep extreme cut: From extreme points to object segmentation. CVPR 2018





Original Image



Person

Bike

Image tags



Bounding

boxes





Scribbles





Points







Convolutional layers

FC Layers







$$CAM_{Dog}(x,y) = \sum_{k} w_{k}^{Dog} A_{k}(x,y) =$$






These activations maps can be used as **pseudo-masks**

• Zhou et al., Learning deep features for discriminative localization. CVPR 2016

Problem: they focus only on highly discriminative regions



Problem: they focus only on highly discriminative regions

Incorporate saliency maps



• Oh et al. Exploiting Saliency for Object Segmentation from Image Level Labels. CVPR 2017

• Fan et al. Learning Integral Objects With Intra-Class Discriminator for Weakly-Supervised Semantic Segmentation. CVPR 2020

Problem: they focus only on highly discriminative regions

Region mining



- Wei et al. Object Region Mining with Adversarial Erasing: A Simple Classification to Semantic Segmentation Approach. CVPR 2017
- Wang et al. Weakly-Supervised Semantic Segmentation by Iteratively Mining Common Object Features. CVPR 2018

CAMs in the medical domain



• Nguyen et al. A novel segmentation framework for uveal melanoma based on magnetic resonance imaging and class activation maps. MIDL 2019.

CAMs in the medical domain



• Chen et al. Exploiting confident information for weakly supervised prostate segmentation based on image-level labels. SPIE Medical Imaging 2020

Knowledge-driven priors

Common priors in natural images

Target Size







- Pathak et al., Constrained convolutional neural networks for weakly supervised segmentation, ICCV 2015
- Xu et al., Learning to Segment Under Various Forms of Weak Supervision, CVPR 2015
- Zhang et al., Curriculum Domain Adaptation for Semantic Segmentation of Urban Scenes. ICCV'17

Knowledge-driven priors

Common priors in natural images

Target Location





- Remez et al. Learning to segment via cut-and-paste. ECCV 2018
- Georgakis et al Synthesizing training data for object detection in indoor scenes. RSS 2017

Knowledge-driven priors

Common priors in natural images

Number of instances







• Deselaers et al. Localizing objects while learning their appearance. ECCV 2010

Knowledge-driven priors

Common priors in natural images

Contrast Foreground/Background



Images from Hou et al, CVPR'17

- Hou et al. Deeply supervised salient object detection with short connections. CVPR 2017
- Li et al. Instance-level salient object segmentation. CVPR 2017

Knowledge-driven priors

Common priors in natural images



Images from the DAVIS Challenge Dataset



- Tokmakov et al. Weakly-supervised semantic segmentation using motion cues. ECCV 2016
- Pathak et al. Learning features by watching objects move. CVPR 2017

What about priors in the medical domain?

Liver #1



Knowledge-driven priors

Anatomical priors

Spleen #2 Pancreas #3

Partial labeled data (exploit target relationships)

Equality constraints





Constrained optimization (in CNNs) Equality constraints Known size Constrain the CNN predictions

Equality constraints (e.g, L2 penalty)



Equality constraints (e.g, L2 penalty)



Equality constraints (e.g, KL)

Unsupervised domain adaptation



Partially labeled data



Equality constraints (e.g, KL): Curriculum DA



Equality constraints (e.g, KL): Curriculum DA



Zhang et al., Curriculum Domain Adaptation for Semantic Segmentation of Urban Scenes. ICCV'17

Equality constraints (e.g, KL): Curriculum DA



Zhang et al., Curriculum Domain Adaptation for Semantic Segmentation of Urban Scenes. ICCV'17

Equality constraints (e.g, KL): Curriculum DA





Zhang et al., Curriculum Domain Adaptation for Semantic Segmentation of Urban Scenes. ICCV'17

Equality constraints (e.g, KL): Curriculum DA





Zhang et al., Curriculum Domain Adaptation for Semantic Segmentation of Urban Scenes. ICCV'17

Equality constraints (e.g, KL): Curriculum DA





Zhang et al., Curriculum Domain Adaptation for Semantic Segmentation of Urban Scenes. ICCV'17

Equality constraints (e.g, KL): Curriculum DA



Equality constraints (e.g, KL): Partial annotations



Equality constraints (e.g, KL): Partial annotations



Figure 1. 3D Visualization of several abdominal organs (liver, spleen, left kidney, right kidney, aorta, inferior vena cava) to show the similarity of patient-wise abdominal organ size distributions.

Equality constraints (e.g, KL): Partial annotations





Equality constraints (e.g, KL): Partial annotations



Prior-aware loss



Equality constraints (e.g, KL): Partial annotations



Prior-aware loss

Embed prior knowledge



[Zhou et al., Prior-aware Neural Network for Partially-Supervised Multi-Organ Segmentation, ICCV'19]

Equality constraints (e.g, KL): Partial annotations



KL can be expanded

$$\sum_{c} KL(q^{c}|\hat{p}^{c}) = -\sum_{c} (q^{c}\log\hat{p}^{c} + ((1-q^{c})\log(1-\hat{p}^{c})) + const$$

Prior-aware loss

$$-\sum_{c=0}^{|K|} \{q^c \log \frac{1}{N} \sum_{p \in \mathcal{P}} \mathbf{s}_{\theta}^{p,c} + (1-q^c) \log(1-\frac{1}{N} \sum_{p \in \mathcal{P}} \mathbf{s}_{\theta}^{p,c})\} + const$$

[Zhou et al., Prior-aware Neural Network for Partially-Supervised Multi-Organ Segmentation, ICCV'19]

Equality constraints (e.g, KL): Partial annotations



Prior-aware loss



Equality constraints (e.g, KL): Partial annotations



Stochastic primal-dual gradient

(split terms updated independently)

Prior-aware loss

KL can be expanded



Equality constraints (e.g, KL): Partial annotations





Stochastic primal-dual gradient

(split terms updated independently)

Prior-aware loss

KL can be expanded



Equality constraints



Extremal perturbations

Equality constraints



Extremal perturbations

- 1 Relax the mask
 - $\mathbf{m} \in [0,1]^{|\Omega|}$
- 2 Vectorize and sort **m** (non-decreasing order)
- 3 If **m** satisfies the area constraints (a) **exactly**

$$\mathbf{r}_{a} \in [0,1]^{|\Omega|} = \underbrace{[0,0,...,0,1,1,...,1]}_{(1-a)|\Omega|}$$

Equality constraints



Extremal perturbations

1 - Relax the mask

 $\mathbf{m} \in [0,1]^{|\Omega|}$

- 2 Vectorize and sort **m** (non-decreasing order)
- 3 If **m** satisfies the area constraints (a) **exactly**

$$\mathbf{r}_{a} \in [0,1]^{|\Omega|} = \underbrace{[0,0,...,0,1,1,...,1]}_{(1-a)|\Omega|}$$

$$R_a(\mathbf{m}) = \|vecsort(\mathbf{m}) - r_a\|^2$$
Equality constraints (at pixel-level)



Spatial priors on GTA5

Equality constraints (at pixel-level)



Objective:

$$-\sum_{p \in \mathcal{L}} l(\mathbf{y}^{p}, s^{p}_{\theta}) - \sum_{q \in \mathcal{U}} \sum_{c=1}^{K} (\hat{y}^{q,c} log(prior^{q,c} s^{q,c}_{\theta}) + w_{c} \hat{y}^{q,c})$$





Equality constraints (at pixel-level)





Zou et al., Unsupervised Domain Adaptation for Semantic Segmentation via Class-Balanced Self-Training, ECCV'18

Equality constraints (at pixel-level)



Objective:



Equality constraints (at pixel-level)

Spatial prior























Inequality constraints

Information is given in the form of image-tags

Suppression

$$\sum_{p \in \Omega} s^{p,c}_{\theta} \leq 0 \quad \forall c \not \in C$$





Inequality constraints

Information is given in the form of image-tags

Inclusion (or existence)

$$\sum_{p \in \Omega} s_{\theta}^{p,c} \ge 1 \quad \forall c \in C$$





Inequality constraints

Information is given in the form of image-tags

Target Size a > 1

$$\sum_{p\in\Omega} s^{p,c}_{\theta} \geq a \quad \forall c \in C$$





How we can benefit from this in the medical domain?



Image-tag information

 $\sum s_{\theta}^{p,c} \le 0$ $p \in \Omega$ For negative image tags



Inequality constraints (e.g, L2 penalty)



Full annotations



Partial annotations for cross-entropy

Inequality constraints (e.g, L2 penalty)

Objective

$$\min_{\boldsymbol{\theta}} \mathcal{H}(S) \quad \text{s.t} \quad a \leq \sum_{p \in \Omega} s_{\boldsymbol{\theta}}^{p,c} \leq b \quad \square \qquad \mathcal{H}(S) + \lambda \mathcal{C}(V_S).$$

Inequality constraints (e.g, L2 penalty)



Inequality constraints (e.g, L2 penalty)



Inequality constraints (e.g, L2 penalty)



Inequality constraints (e.g, L2 penalty)



[Kervadec et al., Curriculum semi-supervised segmentation. MICCAI'19]

Take-home message

 Imposing constraints helps weakly-supervised segmentation learning by restricting plausible segmentations on unlabeled images

• Few constraints have been explored under low-labeled data regime

• Room for improvement (many opportunities)

Thank you!